CASE REPORTS

Sarcoidosis and antiphospholipid syndrome: A rare association

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ABSTRACT

Sarcoidosis is a systemic inflammatory disorder of unknown cause that is characterized by the granulomatous inflammation of various organs. Antiphospholipid syndrome (APS) is an autoimmune condition defined by persistently positive antiphospholipid antibodies as well as recurrent arterial or venous thromboses and pregnancy complications. Several autoimmune diseases have been described in patients with sarcoidosis, however, a possible correlation between sarcoidosis and APS remains unknown. We present the fifth reported case in the literature.

Key Words: Sarcoidosis, Antiphospholipid syndrome, Association, Autoimmune diseases

1. INTRODUCTION

Sarcoidosis is a chronic multisystemic non-caseating granulomatous disease of unknown cause.[1] Antiphospholipid syndrome (APS) is a clinical condition characterized by recurrent thrombotic events and/or pregnancy morbidity associated with the persistence of antiphospholipid antibodies.[2] The relationship of sarcoidosis and APS is not clearly understood and the possibility of these two entities share pathophysiological mechanisms has been explored. Both APS and sarcoidosis have been known to occur with autoimmune conditions[3,4] and even though studies have found an association between antiphospholipid antibodies and sarcoidosis,[5–7] cases with both sarcoidosis and APS are extremely rare.[8–12]

2. CASE PRESENTATION

A 51-year-old white male patient presented to the Internal Medicine consult with a 6-day painless, unilateral swelling of the right lower limb, with no associated signs of inflammation, skin changes or trauma history, and the doppler ultrasound revealed Deep Vein Thrombosis (DVT) at popliteal and femoral veins. The patient's past medical history included hypertension, dyslipidemia, obesity as well as sarcoidosis. The sarcoidosis was diagnosed in 1997 with multiorganic involvement (lung, liver and skin) and hypercalcemia, by performing a liver biopsy that revealed the presence of noncaseating granulomas. The patient was treated with corticosteroids and immunosuppressants for years, but as the patient was asymptomatic, the therapy was discontinued 5 years before the presentation on our consult. After the diagnosis of DVT, the patient was placed on low molecular weight heparin (80 mg twice daily) and investigated. An initial prothrombotic study was made, with positive results for lupus anticoagulant activity, anticardiolipin immunoglobulin M (IgM) antibodies of 54 U/ml (normal range between 0-15 U/ml) and anti-beta2-glicoprotein IgM antibodies also positive of 56.7 U/ml (normal range < 20 U/ml). Antinuclear and Antineutrophil antibodies were negative. Determination

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of C and S Protein, homocystein, antithrombin III, as well as search for factor V Leiden and Prothrombin gene were negative. The prothrombotic study was repeated after 12 weeks, maintaining persistently positive antiphospholipid antibodies, fulfilling the Sapporo criteria for APS. The patient was treated with low molecular weight heparin acutely followed by lifelong warfarin. There weren't reported further thrombotic events while on anticoagulation and the patient remains on follow-up consult, asymptomatic.

3. DISCUSSION

Only four definite cases of APS and sarcoidosis have been reported in the literature.[8] Both APS and sarcoidosis share immune dysregulation and autoimmunity,[3,4] which might explain their co-occurrence.[8] It is thought that an exaggerated cellular immune response in target tissues in patients with sarcoidosis is caused by exposure to an unknown antigen and the antiphospholipid antibody syndrome seems to be mediated by an autoimmune antibody response which leads us to think that a common antigenic stimulus may be in the genesis of both processes.[13] Ina et al. investigated the level of antiphospholipid antibodies in 55 sarcoidosis patients and detected these antibodies in 38% of the sample, describing a correlation between the presence of antiphospholipid antibodies and the existence of sarcoidotic extrathoracic lesions.[7] Diagnosis of APS is made according to the revised Sapporo criteria,[14] which requires at least one clinical (vascular thrombosis or pregnancy morbidity) and one laboratory criteria (presence of lupus anticoagulant and immunoglobulin G [IgG], and/or IgM anticardiolipin antibody, and/or IgG and/or IgM anti-beta 2 glycoprotein antibody). All antibodies must be demonstrated on two or more occasions separated by least 12 weeks, as we described in this clinical case.[8] Our patient has a definite diagnosis of sarcoidosis and fulfills the modified Sapporo criteria for definite APS. It was a male patient, which argues against all the previous four cases described where all the patients were females.[8] Interestingly, DVT is the most common thrombotic complication of APS in a large European cohort[15] and in this case, was the leading thrombotic event. Several reports describe thrombotic events in sarcoidoisis patients, unfortunely the level of antiphospholipid antibody was not measured making it hard to prove the existence of APS.[3] On the other hand, diagnosis of APS in a patient that doesn't have active granulomatous inflammation as in the presented case can argue against a pathophysiological link between this two entities. We agree that further reporting of cases and more pathophysiological studies will help to better define this association, determine if APS is a prognostic marker of sarcoidosis, and provide details on whether treating the underlying sarcoidosis may reduce the thrombotic risk in this subset of APS.[8]

4. CONCLUSION

Sarcoidosis and APS are chronic conditions of immune dysregulation whose etiologies remain mysterious.[16] This case report shows a very rare association that can be either an occasional finding, or, as they can share some pathophysiological mechanisms, have a possible correlation not yet understood. However, APS should be considered as a differential diagnosis in the presence of a thrombotic event in patients with sarcoidosis regardless the activity of the disease. Progressive study of the molecular pathways involved in these diseases and research for antiphospholipid antibodies in patients with sarcoidosis, may reveal more information about shared immunopathologic mechanisms underlying these conditions.

CONFLICTS OF INTEREST DISCLOSURE

The authors have declared no conflicts of interest.

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